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(71) Applicant *(for all designated States except US)*: **JOHNSON & JOHNSON MEDICAL LIMITED** [GB/GB]; Erskine House, 68-73 Queen Street, Edinburgh EH2 4NH (GB).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **ADDISON, Deborah** [GB/GB]; 2 Dovenanter Cottage, Keasden, Near Clapham, Lancaster LA2 8HB (GB). **SILCOCK, Derek, Walter** [GB/GB]; 2 Ash Grove, Skipton BD23 1QP (GB).

(74) Agents: **JAMES, Anthony, Christopher, W., P.** et al.; Carpmaels & Ransford, 43 Bloomsbury Square, London WC1A 2RA (GB).

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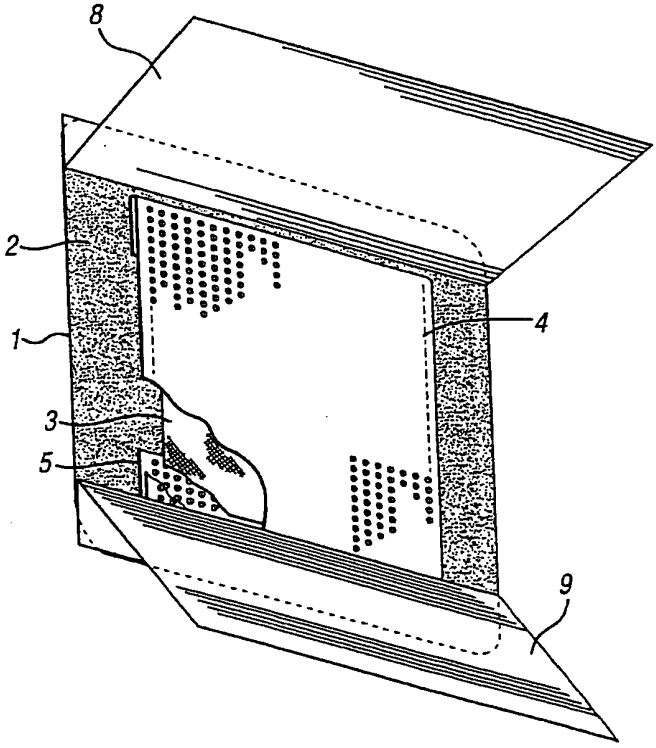
(54) Title: HYDROGEL WOUND DRESSINGS

(57) Abstract: The invention provides a wound dressing comprising: a liquid-permeable top sheet having a wound facing surface and a back surface, said top sheet being adapted to block or restrict passage of liquid from the back surface to the wound facing surface; and an insoluble hydrogel layer on the wound facing surface of the top sheet.



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HYDROGEL WOUND DRESSINGS

The present invention relates to wound dressings incorporating an absorbent structure and a hydrogel layer for the maintenance of a suitable moisture level at the surface of wounds.

It is known that the maintenance of a moist wound environment promotes the healing of wounds, especially burns and chronic wounds such as ulcers. However, it is also desirable to avoid excessive moisture or pooling of wound exudate on the wound, since liquid exudate causes maceration of skin adjacent to the wound and other difficulties. Furthermore, liquid exudate can leak from the wound site and contaminate clothes or bedding.

In practice, it is difficult to maintain the desired moisture level at the wound site because the rate of wound fluid production varies from wound to wound, and over time for any single wound. This can necessitate frequent dressing changes and a range of dressing types to treat different wounds.

It is an object of the present invention to provide structures for use as or in improved multilayer dressings for the treatment of a wide range of wounds.

The present invention provides a wound dressing comprising: a liquid-permeable top sheet having a wound facing surface and a back surface, said top sheet being adapted to block or restrict passage of liquid from the back surface to the wound facing surface; and a hydrogel layer on the wound facing surface of the top sheet.

Preferably, the dressing further comprises a backing layer over the back face of the top sheet. The backing layer supports the top sheet and an intermediate absorbent layer (where present) and preferably provides a barrier to passage of microorganisms through the dressing. The backing layer may extend beyond at least one edge of the absorbent layer to provide an adhesive-coated margin adjacent to the said edge for adhering the dressing to a surface, such as to

the skin of a patient adjacent to the wound being treated. An adhesive-coated margin may extend around all sides of the absorbent layer, so that the dressing is a so-called island dressing. However, it is not necessary for there to be any adhesive-coated margin.

Preferably, the backing layer is substantially liquid-impermeable. The backing sheet is preferably semipermeable. That is to say, the backing sheet is preferably permeable to water vapour, but not permeable to liquid water or wound exudate. Preferably, the backing sheet is also microorganism-impermeable. Suitable continuous conformable backing sheets will preferably have a moisture vapor transmission rate (MVTR) of the backing sheet alone of 300 to 5000 $g/m^2/24hrs$, preferably 500 to 2000 $g/m^2/24hrs$ at 37.5 °C at 100% to 10% relative humidity difference. The backing sheet thickness is preferably in the range of 10 to 1000 micrometers, more preferably 100 to 500 micrometers.

The MVTR of the dressing according to the present invention as a whole is lower than that of the backing sheet alone, because the top sheet partially obstructs moisture transfer through the dressing. Preferably, the MVTR of the dressing (measured across the island portion of the dressing) is from 20% to 80% of the MVTR of the backing sheet alone, more preferably from 20% to 60% thereof, and most preferably about 40% thereof. It has been found that such moisture vapor transmission rates allow the wound under the dressing to heal under moist conditions without causing the skin surrounding the wound to macerate.

Suitable polymers for forming the backing sheet include polyurethanes and poly alkoxyalkyl acrylates and methacrylates such as those disclosed in GB-A-1280631. Preferably, the backing sheet comprises a continuous layer of a high density blocked polyurethane foam that is predominantly closed-cell. A suitable backing sheet material is the polyurethane film available under the Registered Trade Mark ESTANE 5714F.

The adhesive (where present) layer should be moisture vapor transmitting and/or patterned to allow passage of water vapor therethrough. The adhesive layer is preferably a continuous moisture vapor transmitting, pressure-sensitive adhesive layer of the type conventionally used for island-type wound dressings, for example, a pressure sensitive adhesive based on acrylate ester copolymers, polyvinyl ethyl ether and polyurethane as described for example in GB-A-1280631. The basis weight of the adhesive layer is preferably 20 to 250 g/m^2, and more preferably 50 to 150 g/m^2. Polyurethane-based pressure sensitive adhesives are preferred.

Preferably, the adhesive layer extends outwardly from the absorbent layer and the envelope to form an adhesive-coated margin on the backing sheet around the adhesive layer as in a conventional island dressing.

The area of the optional absorbent layer is typically in the range of from 1cm^2 to 200cm^2, more preferably from 4cm^2 to 100cm^2.

The optional absorbent layer may be any of the layers conventionally used for absorbing wound fluids, serum or blood in the wound healing art, including gauzes, nonwoven fabrics, superabsorbents, hydrogels and mixtures thereof. Preferably, the absorbent layer comprises a layer of absorbent foam, such as an open celled hydrophilic polyurethane foam prepared in accordance with EP-A-0541391, the entire content of which is expressly incorporated herein by reference. In other embodiments, the absorbent layer may be a nonwoven fibrous web, for example a carded web of viscose staple fibers. The basis weight of the absorbent layer may be in the range of 50-500g/m^2, such as 100-400g/m^2. The uncompressed thickness of the absorbent layer may be in the range of from 0.5mm to 10mm, such as 1mm to 4mm. The free (uncompressed) liquid absorbency measured for physiological saline may be in the range of 5 to 30 g/g at 25°C.

The optional absorbent layer may additionally comprise one or more active therapeutic or antimicrobial agents. Suitable therapeutic agents include growth

factors, analgesics, local anaesthetics and steroids. Suitable antimicrobial agents include antiseptics such as silver compounds (e.g. silver sulfadiazine) and chlorhexidine, and antibiotics. The therapeutic or antimicrobial agents are usually added in an amount of from 0.01% to 5% by weight, based on the dry weight of the absorbent layer. Provision of the antimicrobial in the absorbent layer may be preferable for two reasons (1) Simple manufacturing route, and (2) Having the antimicrobial away from the wound would prevent unnecessary exposure to the antimicrobial when it may not be needed, e.g. drier wounds. In the presence of higher exudate, higher levels of the antimicrobial will be released as the absorbent layer becomes wet. Whilst the directional top sheet should restrict the flow of exudate back to the wound (to some extent through surface tension of the liquid), the antimicrobial should go against the concentration gradient and pass back through the perforated sheet and into the wound. It is know that antimicrobial components such as silver ions can be transported through relatively low levels of moisture.

The top sheet of the wound dressing according to the invention is liquid permeable, but acts to block or restrict the flow of liquid from the back surface to the wound site. That is to say, the top sheet allows fluid to pass through the top sheet from the wound site, but blocks or restricts flow of the fluid back through the top sheet onto the wound (also known as wet-back). Such non-wetting or top sheets may for example be made from porous non-woven fabrics comprising a layer of hydrophobic fibers, or having a hydrophobic finish applied to at least the outer surface thereof. Preferably, the top sheet has greater liquid permeability to the flow of liquid away from the wound facing surface than to the flow of liquid towards the wound facing surface.

Preferably, the top sheet is formed from a substantially liquid-impermeable sheet material provided with tapered capillaries, each capillary having a base substantially in the plane of the wound facing surface of the top sheet and an apical opening remote from the wound facing surface of the top sheet and preferably in contact with an absorbent layer. The conical capillaries provide

rapid one-way wicking of fluid from the front of the top sheet, with minimal wet-back. Top sheets of this type are described in GB-A-1526778.

The top sheet film may be formed from a thermoplastic film-forming polymer. Preferably, the polymer is conformable but not substantially elastomeric. Suitable polymers include, but are not limited to, polyethylene, polypropylene, polyester, polyamides such as nylons, fluoropolymers such as polyvinylidene fluoride (PVDF) or polytetrafluoroethylene (PTFE), and mixtures thereof. The top sheet is preferably a polyolefin film. Preferably, the film has a thickness by weight (ASTM E252-84) of from 10 to 200 micrometers, more preferably from 25 to 100 micrometers.

Preferably, the capillaries are substantially in the form of truncated cones. Preferably, the capillaries have a base opening dimension (the maximum opening dimension in the plane of the top sheet) of from 0.1 mm to 3 mm, and an apical opening dimension (remote from the plane of the top sheet) of from 0.05 to 2 mm. More preferably, the capillaries have a base opening dimension as herein defined of from 0.3 mm to 1 mm, and an apical opening dimension of from 0.1 to 0.5 mm.

Preferably, the capillaries have an average angle of taper (measured from the perpendicular to the plane of the top sheet) of from 10 to 60 degrees. Preferably, the embossed thickness of the top sheet (by ASTM D374-79) is from 0.2 to 2 mm, more preferably from 0.4 to 1 mm.

Top sheets of this type may be manufactured, for example, by embossing or vacuum perforation of a liquid-impermeable thermoplastic film. Preferably, the density of the capillaries is from 10 to 400 per cm^2, more preferably from 50 to 200 per cm^2. Preferably, the open area of the top sheet is from 5 to 50% of the total area, more preferably from 10 to 25% of the total area.

It has now been found, surprisingly, that the application of a hydrogel layer to the top surface of such a top sheet enables a moist wound environment to be maintained for prolonged periods, over a wide range of wound exudation rates.

The top sheet continues to wick away wound fluid to prevent excessive moisture in the wound, but this does not result in removal of the hydrogel or blocking of the top sheet by the hydrogel. When the rate of wound exudate production falls, the hydrogel absorbs moisture vapor from the absorbent layer and preserves a moist wound contacting surface. The hydrogel does not give rise to substantially increased wet-back through the top sheet.

Preferably, the hydrogel layer has a dry basis weight of from 10 to 200g/m^2, more preferably from 10 to 100g/m^2, and most preferably from 10 to 50g/m^2.

The term "hydrogel layer" refers generally to layers that interact with the wound surface under physiological conditions to maintain an elevated moisture level at the wound surface. Preferably, the hydrogel layer forms a gel with water under physiological conditions of temperature and pH. Such hydrogel layers can be formed by the inclusion of medically acceptable macromolecular materials that preferably have the ability to swell and absorb fluid while maintaining a strong integral structure. The hydrogel material is substantially insoluble in water under physiological conditions, whereby the hydrogel is not washed away by the wound fluid. The hydrogel may be a biopolymer, and/or it may be bioabsorbable. That is to say, it may undergo gradual resorption *in vivo*.

Exemplary insoluble gels include certain cross-linked polyacrylate gels, calcium alginate gels, cross-linked hyaluronate gels, wherein the hydrogel layer comprises a hydrogel material selected from gels formed from vinyl alcohols, vinyl esters, vinyl ethers and carboxy vinyl monomers, meth(acrylic) acid, acrylamide, N-vinyl pyrrolidone, acylamidopropane sulphonic acid, PLURONIC (Registered Trade Mark) (block polyethylene glycol, block polypropylene glycol) polystyrene-, maleic acid, NN-dimethylacrylamide diacetone acrylamide, acryloyl morpholine, and mixtures thereof. Preferably, the gel adheres strongly to the surface of the top sheet material to resist washing off by wound fluid. In certain embodiments the gel may be chemically bonded to the surface of the top sheet.

Preferably, the hydrogel layer comprises a hydrogel material selected from polyurethane gels, biopolymer gels, carboxymethyl cellulose gels, hydroxyethyl cellulose gels, hydroxy propyl methyl cellulose, modified acrylamide and mixtures thereof. Suitable biopolymer gels include alginates, pectins, galactomannans, chitosan, gelatin, hyaluronates and mixtures thereof. Some of these biopolymer materials also promote wound healing.

Preferably, the gels are cross-linked, and the cross-linking may be either covalent or ionic.

Preferably, the hydrogel material further comprises from 5 to 50% by weight on a dry weight basis of one or more humectants such as glycerol.

Preferably, the hydrogel layer comprises a hydrogel material of the kind described in WO00/07638, the entire contents of which is incorporated herein by reference.

Alternatively or additionally to the gel-forming macromolecules, the hydrogel layer may comprise one or more emollients. Emollients are used to smooth the surface of skin and to increase the degree of hydration. They act either by occluding water loss from the outer layer of the skin, or by improving water binding to the skin. Emollients are particularly useful in the treatment of atopic eczemas and ichthyoses. Preferred emollients include White Soft Paraffin, Yellow Soft Paraffin, Liquid paraffin, Urea Creams, Lanolin, Sodium Pyrrolidone Carboxylate (PCA Na), Evening primrose extract (gamma linolenic acid), Soya Oil, Tea Tree Oil, Coconut Oil, Almond Oil, Camomile Extract, Cod Liver Oil, Peanut Oil, Emu Oil, Aloe Vera, Sunflower oil, Avocado Oil, Jojoba Oil, Cocoamide, and mixtures thereof.

The hydrogel layer may additionally comprise one or more active therapeutic or antimicrobial agents. Suitable therapeutic agents include growth factors, analgesics, local anaesthetics and steroids. Suitable antimicrobial agents include antiseptics such as silver compounds (e.g. silver sulfadiazine) and

chlorhexidine, and antibiotics. The therapeutic or antimicrobial agents are usually added in an amount of from 0.01% to 5% by weight, based on the dry weight of the hydrogel layer.

The hydrogel layer may be continuous or discontinuous, but in any case is preferably apertured in register with the capillaries in the top sheet so as not to obstruct passage of fluid into the capillaries even when the hydrogel is fully swelled. In other words, there is preferably substantially no hydrogel initially present in or covering the capillaries of the top sheet. The hydrogel layer may be applied by spraying or, preferably, by a printing or transfer process.

Preferably, the multilayer wound dressing according to the invention further comprises one or more protective cover sheets over the hydrogel layer and any exposed adhesive. For example, these may comprise one or more release-coated paper cover sheets. Preferably, the dressing is sterile and packaged in a microorganism-impermeable container.

The present invention further provides the use of a multilayer wound dressing according to the present invention for the preparation of a dressing for application to a wound.

In a further aspect, the present invention provides a method of treatment of a wound comprising the step of applying a dressing in accordance with the present invention to the surface of the wound with the hydrogel contacting the wound.

An embodiment of the present invention will now be described further, by way of example, with reference to the accompanying drawings, in which:

Figure 1 shows a perspective view of the lower (wound contacting) surface of a wound dressing according to the invention; and

Figure 2 shows a partial transverse cross section (not to scale) through the island region of the dressing of Figure 1.

Referring to Figure 1, the wound dressing is an island-type self-adhesive wound dressing comprising a backing layer 1 of microporous liquid-impermeable polyurethane foam, such as ESTANE 5714F (Registered Trade Mark). The backing layer is permeable to water vapor, but impermeable to wound exudate and microorganisms.

The backing layer 1 is coated with a substantially continuous layer 2 of pressure-sensitive polyurethane adhesive.

The absorbent layer 3 is a layer of hydrophilic polyurethane foam prepared as described in EP-A-0541391 and having a basis weight of about 350g/m^2 and a thickness of about 1.5 mm.

The top sheet 4 extends over the absorbent layer 3 and is wrapped partially around the absorbent layer 3 and the edges 5 of the top sheet are adhered to the backing layer 1 behind the absorbent layer 3 by the adhesive 2. This can be seen more clearly in Figure 2. The top sheet is a polyethylene film that has been perforated with about 90 perforations per cm^2, each perforation having a substantially conical shape as hereinbefore described, a maximum hole diameter of about 0.5 mm, an open area of 16% of the total area of the front face, a thickness by weight of about 43 micrometers and an embossed thickness of about 0.5 mm. Such top sheets are available from Tredegar Film Products, Richmond, Virginia under the Registered Trade Mark VISPORE.

Referring to Figure 2, the top sheet 4 presents a smooth, perforated top surface to the wound This surface is coated with a layer of hydrogel 6 applied by spraying that is apertured in register with the capillaries in the top sheet to allow passage of fluid into the capillaries even when the hydrogel is fully swelled. The hydrogel 6 has a dry basis weight of 30g/m^2 and consists of bovine gelatin cross-linked with glutaraldehyde or formaldehyde.

The wound facing surface of the dressing shown in Figure 1 is protected by two silicone-coated release papers 8,9, packed in a microorganism-impermeable pouch, and sterilised using gamma radiation.

In use, the dressing is removed from the package, the release papers are removed, and the dressing is adhered to the skin around the wound with the top sheet and hydrogel in contact with the wound to provide a sterile and absorbent dressing. The hydrogel and top sheet interact in hitherto unexpected ways to provide a moist but not wet wound environment for a wide range of wounds over an extended period.

The above embodiment has been described by way of example only. Many other embodiments falling within the scope of the accompanying claims will be apparent to the skilled reader.

CLAIMS

1. A wound dressing comprising: a liquid-permeable top sheet having a wound facing surface and a back surface, said top sheet being adapted to block or restrict passage of liquid from the back surface to the wound facing surface; and a hydrogel layer on the wound facing surface of the top sheet.

2. A wound dressing according to claim 1, further comprising an absorbent layer in contact with the back surface of the top sheet.

3. A wound dressing according to any preceding claim, wherein the absorbent layer comprises a layer of hydrophilic foam, a superabsorbent, or a combination thereof.

4. A wound dressing according to claim 2 or 3, wherein the absorbent layer further comprises a medicament.

5. A wound dressing according to any preceding claim, wherein the dressing further comprises a substantially liquid-impermeable backing layer over the absorbent layer.

6. A wound dressing according to claim 5, further comprising a layer of adhesive on the surface of the backing layer facing the top sheet.

7. A wound dressing according to claim 6, wherein the backing layer extends beyond at least one edge of the absorbent layer to provide an adhesive-coated margin adjacent to said edge for adhering the dressing to a surface.

8. A wound dressing according to any preceding claim, wherein the top sheet comprises a porous, substantially hydrophobic, non-woven fabric.

9. A wound dressing according to any preceding claim, wherein the top sheet is formed from a liquid-impermeable sheet material provided with tapered

capillaries, each capillary having a base substantially in the wound facing surface of the top sheet and an apical opening remote from the plane of the top sheet and in contact with the absorbent layer.

10. A wound dressing according to claim 9, wherein the capillaries are substantially in the form of truncated cones.

11. A wound dressing according to claim 9 or 10, wherein the capillaries have a base opening dimension as herein defined of from 0.15 mm to 6 mm, and an apical opening dimension of from 0.1 to 2.5 mm.

12. A wound dressing according to claim 11, wherein the capillaries have a base opening dimension as herein defined of from 0.5 mm to 1.5 mm, and an apical opening dimension of from 0.1 to 0.5 mm.

13. A wound dressing according to any of claims 9 to 12, wherein the capillaries have an average angle of taper as herein defined of from 10 to 60 degrees.

14. A wound dressing according to any preceding claim, wherein the hydrogel layer has a dry basis weight of from 10 to 200g/m^2.

15. A wound dressing according to any preceding claim, wherein the hydrogel layer comprises a hydrogel material selected from polyurethane gels, biopolymer gels, carboxymethyl cellulose gels, hydroxyethyl cellulose gels hydroxypropyl methyl cellulose, modified acrylamides and mixtures thereof.

16. A wound dressing according to any preceding claim, wherein the hydrogel layer comprises a hydrogel material selected from gels formed from vinyl alcohols, vinyl esters, vinyl ethers and carboxy vinyl monomers, meth(acrylic) acid, acrylamide, N-vinyl pyrrolidone, acylamidopropane sulphonic acid, pluronic (block polyethylene glycol, block polypropylene glycol)polystyrene maleic acid, NN-dimethylacrylamide, diacetone acrylamide or acryloyl morpholine.

17. A wound dressing according to any preceding claim, wherein the hydrogel layer comprises an emollient.

18. A wound dressing according to claim 17, wherein the emollient is selected from the group consisting of white soft paraffin, yellow soft paraffin, liquid paraffin, urea creams, lanolin, sodium pyrrolidone carboxylate, evening primrose extract (gamma linolenic acid), soya oil, tea tree oil, coconut oil, almond oil, camomile extract, cod liver oil, peanut oil, emu oil, aloe vera, sunflower oil, avocado oil, jojoba oil, cocoamide, and mixtures thereof.

19. A wound dressing according to any preceding claim, wherein the hydrogel layer comprises an active therapeutic agent or an antimicrobial agent.

20. A wound dressing according to claim 19, wherein the hydrogel layer comprises a silver compound.

21. A wound dressing according to any preceding claim, wherein the hydrogel layer is apertured in register with apertures in the top sheet.

22. A wound dressing according to any preceding claim, further comprising one or more protective cover sheets over the hydrogel layer.

23. A wound dressing according to any preceding claim, wherein the dressing is sterile and packaged in a microorganism-impermeable container.

24. Use of a wound dressing according to any preceding claim for the preparation of a dressing for application to a wound.

FIG. 1

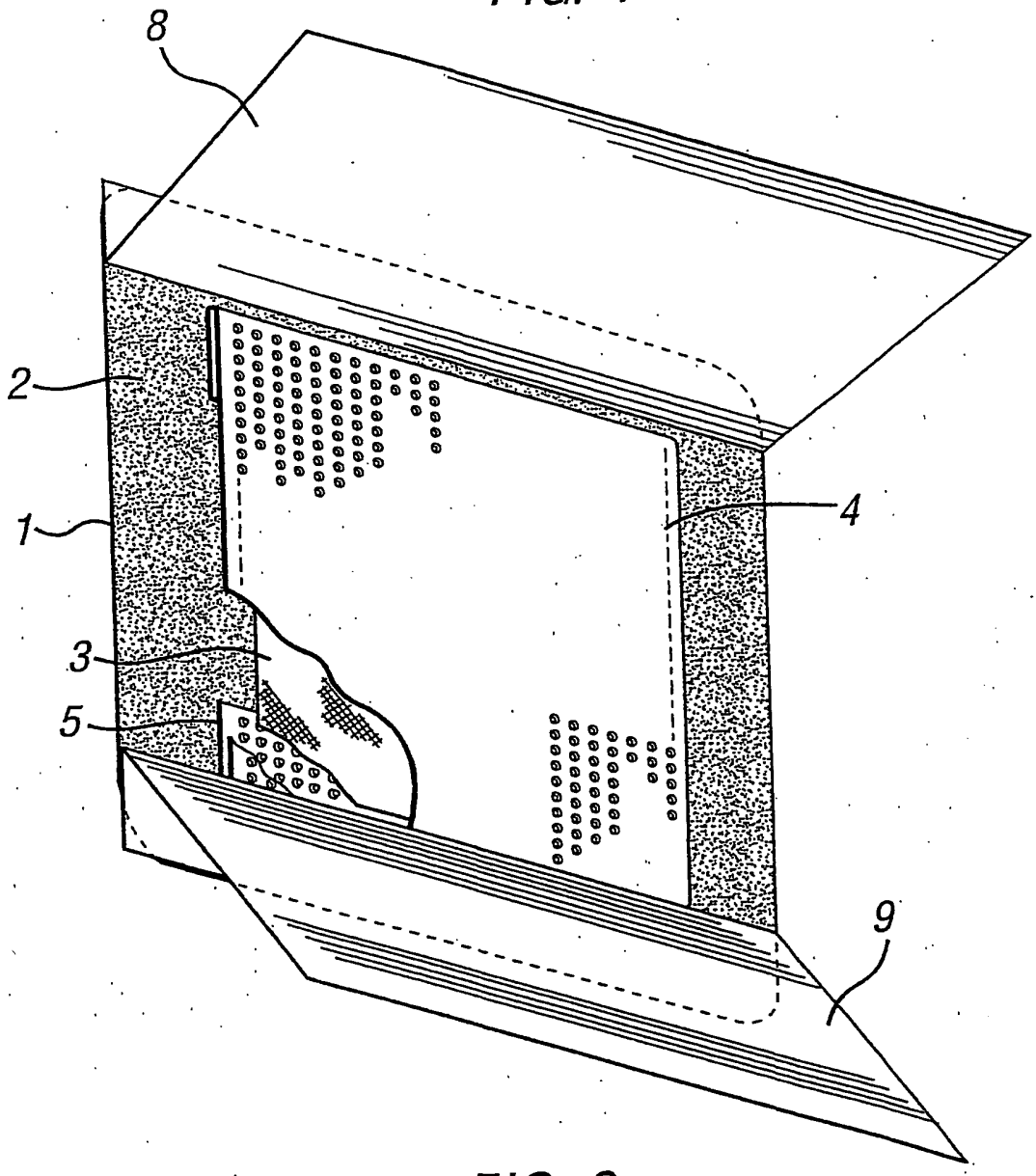
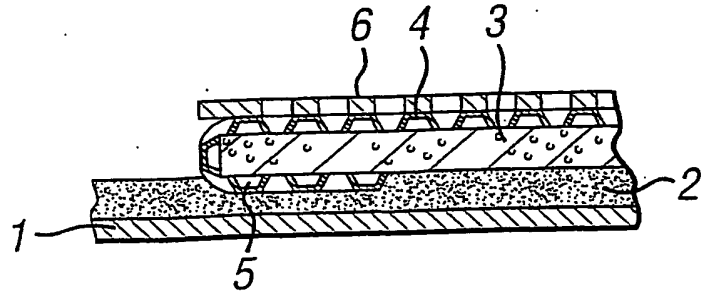


FIG. 2



INTERNATIONAL SEARCH REPORT

Inte nal Application No
PCT/GB 01/04983

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61F13/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 010 883 A (POTTER WILLIAM D ET AL) 30 April 1991 (1991-04-30) column 1, line 10 - line 35 column 5, line 35 -column 8, line 68 column 9, line 25 -column 10, line 39	1-7, 21-24
Y	column 11, line 54 -column 12, line 49; claims; figures	8-20
Y	US 3 929 135 A (THOMPSON HUGH ANSLEY) 30 December 1975 (1975-12-30) cited in the application column 4, line 1 - line 62; figures	8-14

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

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Date of the actual completion of the international search	Date of mailing of the international search report
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Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 01/04983

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4 990 144 A (BLOTT PATRICK L) 5 February 1991 (1991-02-05) column 1, line 21 -column 2, line 53 column 5, line 4 -column 6, line 39 claims; figures	15-20
A	US 5 204 110 A (ALLAIRE MICHAEL J ET AL) 20 April 1993 (1993-04-20) column 5, line 22 -column 7, line 63	1,14-16
A	US 4 341 207 A (STEER PETER L ET AL) 27 July 1982 (1982-07-27) the whole document	1-24
A	US 5 423 736 A (WOLF MICHAEL L ET AL) 13 June 1995 (1995-06-13) claims; figures	1-24
A	US 5 540 922 A (FABO TOMAS) 30 July 1996 (1996-07-30) claims; figures	1-24
A	US 5 465 735 A (PATEL HARISH A) 14 November 1995 (1995-11-14) claims; figures	1,9
A	EP 0 536 875 A (NDM ACQUISITION CORP) 14 April 1993 (1993-04-14) claims; figures	1-24
A	US 5 501 661 A (CARTMELL JAMES V ET AL) 26 March 1996 (1996-03-26) claims; figures	1-24

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter nal Application No
PCT/GB 01/04983

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5010883 A	30-04-1991	AT 60897 T	15-03-1991
		AU 566415 B2	22-10-1987
		AU 3684084 A	27-06-1985
		CA 1290210 A1	08-10-1991
		DE 3484133 D1	28-03-1991
		EP 0147119 A2	03-07-1985
		JP 1857260 C	07-07-1994
		JP 5055144 B	16-08-1993
		JP 60222054 A	06-11-1985
		NZ 210533 A	31-07-1987
		ZA 8409752 A	31-07-1985
US 3929135 A	30-12-1975	AT 369238 B	10-12-1982
		AT 587078 A	15-05-1982
		AT 351156 B	10-07-1979
		AT 945975 A	15-12-1978
		AU 8709175 A	02-06-1977
		BE 836857 A1	21-06-1976
		BR 7508479 A	24-08-1976
		CA 1058801 A1	24-07-1979
		CH 595830 A5	28-02-1978
		DE 2556501 A1	01-07-1976
		DK 583675 A ,B,	21-06-1976
		ES 217535 Y	01-03-1977
		FI 753610 A ,B,	21-06-1976
		FR 2294656 A1	16-07-1976
		GB 1526778 A	27-09-1978
		IE 41963 B1	07-05-1980
		IT 1051534 B	20-05-1981
		JP 1133476 C	27-01-1983
		JP 51108943 A	27-09-1976
		JP 57017081 B	08-04-1982
		LU 74067 A1	11-11-1976
		MX 144813 A	24-11-1981
		NL 7514895 A ,C	22-06-1976
		SE 7514345 A	21-06-1976
		ZA 7507380 A	26-01-1977
US 4990144 A	05-02-1991	AT 106710 T	15-06-1994
		AU 601471 B2	13-09-1990
		AU 7719087 A	25-02-1988
		CA 1323268 A1	19-10-1993
		DE 3789998 D1	14-07-1994
		DE 3789998 T2	12-01-1995
		EP 0256893 A2	24-02-1988
		ES 2054680 T3	16-08-1994
		GB 2194446 A ,B	09-03-1988
		IE 61186 B	19-10-1994
		JP 2513712 B2	03-07-1996
		JP 63051865 A	04-03-1988
		ZA 8706101 A	22-02-1988
US 5204110 A	20-04-1993	US 5115801 A	26-05-1992
		AT 123402 T	15-06-1995
		AU 620750 B2	20-02-1992
		AU 7026991 A	07-11-1991
		CA 2035490 A1	03-11-1991
		DE 69110193 D1	13-07-1995

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int ›nal Application No
PCT/GB 01/04983

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5204110 A		DE 69110193 T2	19-10-1995
		EP 0455324 A1	06-11-1991
		JP 1988560 C	08-11-1995
		JP 4227259 A	17-08-1992
		JP 7024671 B	22-03-1995
		NZ 237005 A	28-04-1993
US 4341207 A	27-07-1982	AU 537462 B2	28-06-1984
		AU 6159780 A	09-04-1981
		CA 1151041 A1	02-08-1983
		DE 3065372 D1	24-11-1983
		DK 379780 A ,B,	08-03-1981
		EP 0026572 A1	08-04-1981
		GB 2061732 A ,B	20-05-1981
		IE 50352 B1	02-04-1986
		IL 60976 A	30-09-1983
		JP 1009864 B	20-02-1989
		JP 1524684 C	12-10-1989
		JP 56045667 A	25-04-1981
		NO 802603 A	09-03-1981
		ZA 8005066 A	26-08-1981
US 5423736 A	13-06-1995	US 5429589 A	04-07-1995
		AT 149086 T	15-03-1997
		AU 2606192 A	07-10-1993
		CA 2080497 A1	03-10-1993
		DE 69217651 D1	03-04-1997
		DE 69217651 T2	06-11-1997
		DK 567704 T3	25-08-1997
		EP 0567704 A1	03-11-1993
		JP 6285145 A	11-10-1994
		NZ 244513 A	24-02-1995
		US 5695456 A	09-12-1997
		US 5478308 A	26-12-1995
		US 5762620 A	09-06-1998
		US 5899871 A	04-05-1999
		ZA 9207575 A	10-05-1993
US 5540922 A	30-07-1996	SE 500973 C2	10-10-1994
		DE 69305735 D1	05-12-1996
		DE 69305735 T2	06-03-1997
		EP 0633758 A1	18-01-1995
		ES 2093420 T3	16-12-1996
		JP 7505310 T	15-06-1995
		SE 9200984 A	01-10-1993
		WO 9319710 A1	14-10-1993
US 5465735 A	14-11-1995	NONE	
EP 0536875 A	14-04-1993	US 5160328 A	03-11-1992
		AU 641322 B2	16-09-1993
		AU 1945792 A	11-02-1993
		CA 2073274 A1	08-02-1993
		EP 0536875 A1	14-04-1993
		JP 1998476 C	08-12-1995
		JP 5184621 A	27-07-1993
		JP 7034812 B	19-04-1995
		NZ 243404 A	26-08-1994

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inte nal Application No
PCT/GB 01/04983

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0536875 A		ZA 9204900 A	28-04-1993
US 5501661 A	26-03-1996	US 5476443 A	19-12-1995
		US 5423737 A	13-06-1995
		AU 667766 B2	04-04-1996
		AU 5644794 A	08-12-1994
		CA 2119731 A1	28-11-1994
		EP 0630629 A1	28-12-1994
		JP 2604542 B2	30-04-1997
		JP 7088131 A	04-04-1995
		NZ 250994 A	26-09-1995
		US 5489262 A	06-02-1996